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Abstract: Purpose of review: To examine the recent literature concerning the neural basis and clinical evidence for the response of the labyrinth to sound and vibration: vestibular-evoked myogenic potentials (VEMPs) and vibration-induced nystagmus (VIN). Recent findings: There are two streams of information from each otolith - a sustained stream (afferents with regular resting activity, signalling gravity and low-frequency linear accelerations) and a transient stream (afferents with irregular resting activity) signalling onset of linear acceleration, and sound and vibration. These irregular neurons are synchronized to each cycle of the stimulus. Neurons in the transient stream are tested by presenting sounds or vibration (500 Hz) and using surface electrodes to measure myogenic potentials from muscles activated by otolithic stimuli (VEMPs). 100 Hz vibration activates irregular canal afferents and causes a stimulus-locked VIN in patients with asymmetric canal function. These new tests of the transient system have one big advantage over older tests of the sustained system - they reliably show the effect of long-term unilateral vestibular loss. Summary: The new physiological and anatomical evidence shows how sound and vibration activate otolith and canal receptors and so provides the scientific foundation for VEMPs and VIN, which are important tools for diagnosing vestibular disorders. VIDEO ABSTRACT: http://links.lww.com/CONR/A47.

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Physiology, clinical evidence and diagnostic relevance of sound-induced and vibration-induced vestibular stimulation

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Summary
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Video abstract
http://links.lww.com/CONR/A47.

Keywords
cervical vestibular-evoked myogenic potential, ocular vestibular-evoked myogenic potential, otolith, vestibular, vestibular-evoked myogenic potential, vibration-induced nystagmus

INTRODUCTION

Sound and vibration are regarded as the natural stimuli for the cochlea, but evolution provides a different perspective which helps explain why sound and vibration are now widely used for testing vestibular function. Vestibular hair cells (VHCs) are the evolutionary precursors of cochlear receptor hair cells [1,2] with similar structure, physiology and even sensitivity with thresholds of nanometers of hair-bundle displacement [3]. The cochlea provides sensitive responses to air-conducted sound (ACS) or bone-conducted vibration (BCV), whereas it appears that the vestibular labyrinth has evolved to 'protect' semicircular canal (SCC) receptors from being activated by these same stimuli. The otoliths are an exception: they have very sensitive responses to BCV (higher thresholds to ACS) [4,5▪]. The apparent 'protection' of the SCCs is defeated if there is a defect in the wall of the bony canal, a superior canal dehiscence (SCD): then canal neurons as well as

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KEY POINTS

- High-frequency (500 Hz) bone-conducted vibration selectively activates irregular otolithic but not canal afferents. Each cycle is the effective stimulus.
- Low-frequency (100 Hz) vibration activates both otolith and canal afferents.
- Ocular VEMPs to sound and vibration reflect mainly utricular function, whereas cervical VEMPs to sound and vibration reflect mainly saccular function.
- Superior canal dehiscence enhances vestibular responses to sound and vibration, so that previously unresponsive canal neurons are activated at high frequencies.
- Low-frequency vibration activates irregular horizontal canal afferents and, in patients with unilateral loss, causes VIN which reflects asymmetrical horizontal canal function.

otolith neurons respond to ACS and BCV [6▪,7]. These facts underpin the present use of ACS and BCV in clinical testing of vestibular function.

VESTIBULAR-EVOKED MYOGENIC POTENTIALS

The most widely used clinical tests of otolith function are vestibular-evoked myogenic potentials (VEMPs) because they are such fast simple tests of dynamic otolith function. VEMPs are small myogenic potentials evoked by brief repeated ACS or BCV stimuli recorded by surface electrodes (Fig. 1). The ocular VEMP (oVEMP) is an excitatory potential recorded over the tensed contralateral inferior oblique muscle as the individual looks up: it originates predominantly from afferents from the contralateral utricular macula. The cervical VEMP (cVEMP) is an inhibitory potential recorded over the tensed sternocleidomastoid muscle (SCM): it originates predominantly from afferents from the ipsilateral saccular macula ([5▪] for summaries). Reviews provide full details of the stimuli for clinical testing: recording montage, artifacts, control data, clinical interpretation and guidelines [8▪,9,10▪▪,11▪▪,12,13▪▪,14].

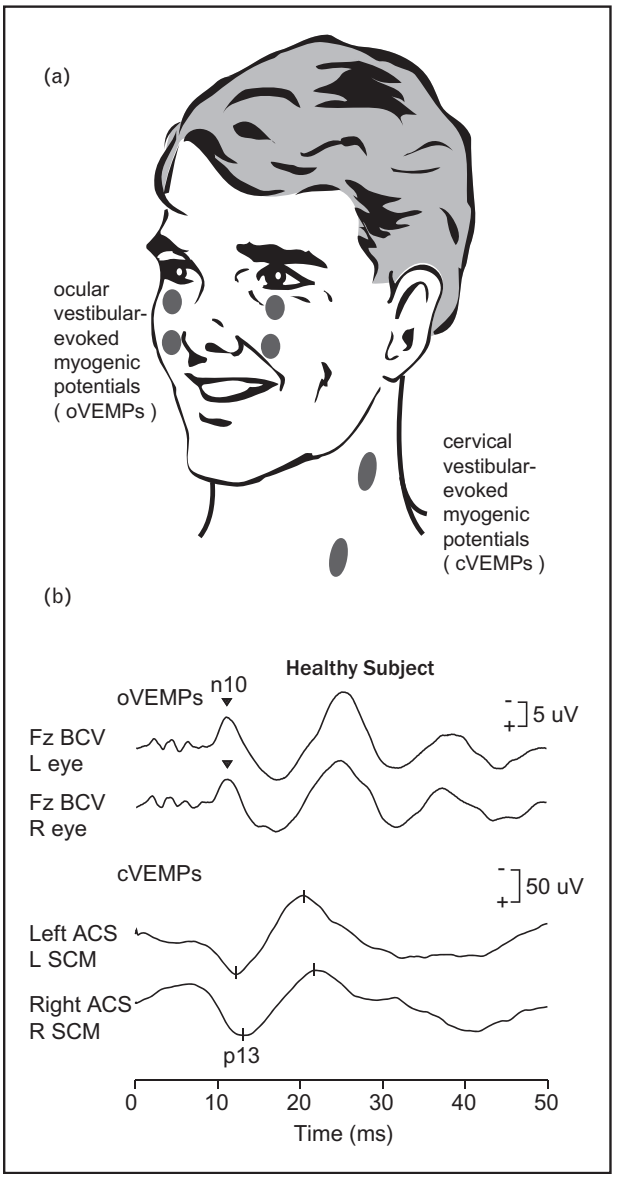

FIGURE 1. In humans electrodes (a) over the inferior oblique eye muscle record the ocular vestibular-evoked myogenic potential, and the n10 component (b) is shown by the inverted caret. Electrodes over the tensed sternocleidomastoid muscle (a) record the cervical vestibular-evoked myogenic potential and the p13 is shown by a dash (b). Fz BCV (Fz bone-conducted vibration) refers to the fact that the bone-conducted vibration stimulus was delivered to the midline of the forehead at the hairline, and this location is known as Fz. (a) Reproduced with permission [8▪]. (b) Reprinted with permission from Elsevier [15].

The anatomical and physiological basis

In both otoliths and SCCs there are two types of receptors – amphora-shaped type I VHCs enveloped by a special calyx afferent ending, and barrel-shaped type II receptors contacted by small bouton afferent endings (Fig. 2) [16]. The distribution of these receptors across the utricular and saccular maculae is not uniform [17▪▪], and there are corresponding physiological variations in afferent neuron physiology [5▪,7,8▪]. The receptors at a particular band in each otolithic macula, the striola, have short stiff hair bundles which are only tenuously attached to

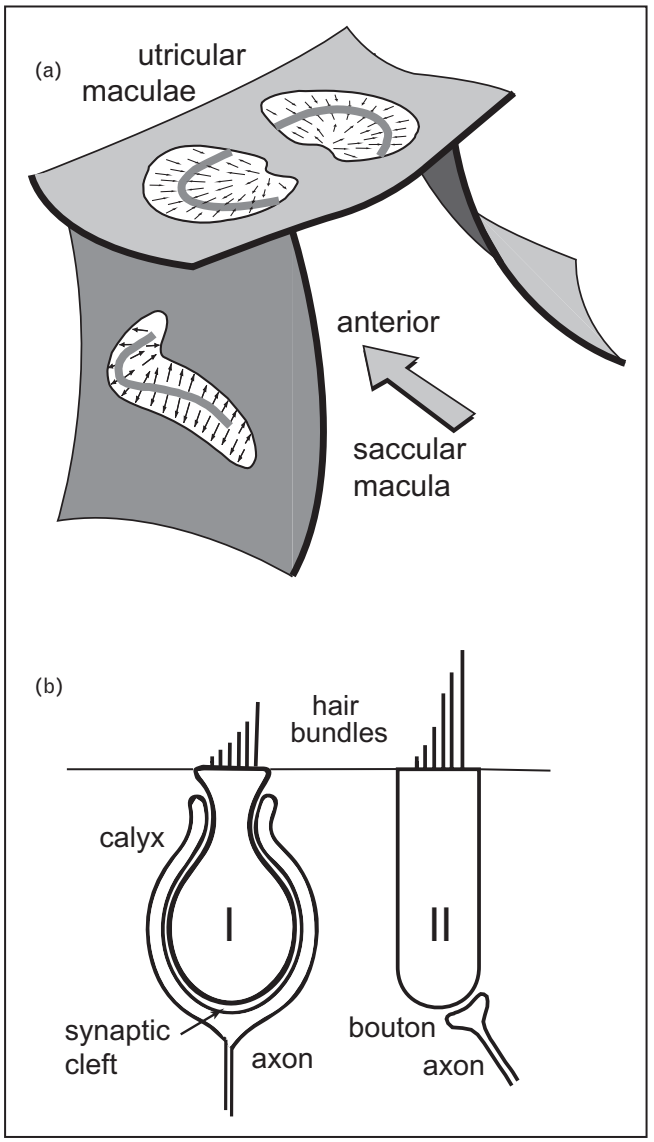

FIGURE 2. Simplified schematics of the approximate spatial organization of the utricular and saccular maculae and the two types of otolithic receptors (types I and II). (a) The small arrows represent the preferred directions of each receptor; the systematic change in preferred direction and the opposite polarization on either side of the line of polarity reversal are shown. The two maculae are mirror images of one another. The band around the line of polarity reversal is called the striola, and irregular otolithic afferents sensitive to sound and vibration synapse on receptors in this band [5▪]. (b) The two types of otolithic receptors – the amphora-shaped type I and the barrel-shaped type II. The afferent fibre forms a calyx ending which envelops the whole type I receptor, whereas for type II receptors the afferent fibre makes a bouton termination on the receptor. (a and b) Adapted with permission [8▪].

the overlying otolithic membrane. The afferents from the striolar type I receptors have irregular resting discharge and can be activated by high-frequency ACS and BCV (e.g. 500 Hz is an optimal stimulus) [5▪,7,18]. Other afferents from all over the otolithic macula have regular resting discharge and synapse on type I and type II receptors with bouton endings, but do not respond to sound and vibration at clinically practical levels [18] (Fig. 2).

When activated by ACS or BCV, irregular otolithic afferents show precise synchronization (phase-locking) of their action potentials to narrow phase bands of the imposed stimulus, even up to frequencies in the kilohertz range [5▪,19] (Fig. 3). Phase-locking implies that the receptor hair-bundles are deflected (and activated) on every single cycle of the stimulus waveform, even up to 3000 Hz. New evidence confirms that during ACS and BCV stimulation the utricular macula moves at the stimulus frequency and the utricular microphonic, generated by the receptor hair cells (the utricular analogue of the cochlear microphonic), can be recorded up to more than 3000 Hz, which shows that the otolithic receptors are being activated by these deflections up to such very high frequencies [20,21].

Modelling [23] reconciles the low-frequency otolithic response to maintained tilts and the high-frequency vibration response by showing that at low frequencies the otoliths function as accelerometers with the otoconia being displaced relative to the receptors, but at high frequencies the otoliths function as seismometers, with the otoconia probably remaining relatively fixed while the macula (and the receptors at the striola) move relative to the otoconia. So, for both low and high frequencies, the receptor hair bundles are deflected, and receptor and afferent activation takes place. Regular afferents do not respond to ACS or BCV but have a strong response to low frequencies of linear accelerations, such as tilts.

In sum, from each sense organ there are parallel streams of neural information: the fast transient stream from irregular afferents signalling dynamic responses (changes in stimulation such as caused by ACS and BCV) and the slower sustained stream from regular afferents signalling maintained or low-frequency acceleration [18]. oVEMPs test dynamic utricular function, but the absence of oVEMPs does not necessarily have any implication about static utricular function, which is tested by maintained otolithic stimuli [with clinical tests such as the subjective visual vertical (SVV) [24▪▪]]. For example, in some cases of intratympanic gentamicin treatment (which selectively attacks type I receptors [25]), the transient function is lost (and so absent oVEMPs); however, the sustained function remains, with the SVV relatively unaffected. Cherchi [26▪▪] has reported exactly this dissociation between dynamic and static tests of utricular function [27▪▪].

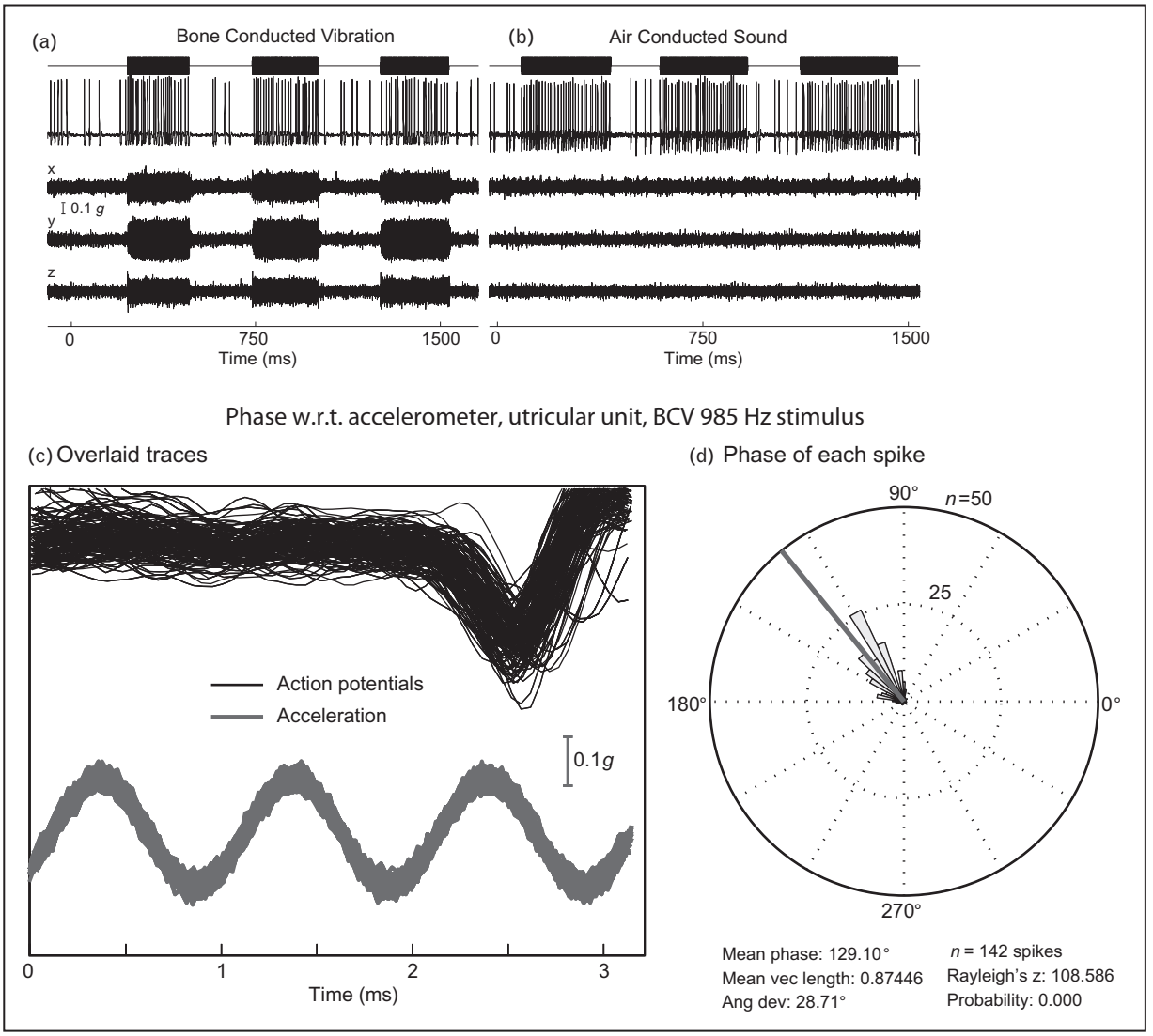

FIGURE 3. Time series of firing of one guinea-pig irregular otolith neuron during stimulation by 500 Hz bone-conducted vibration (a) and air-conducted sound (b) showing that both stimuli cause stimulus-locked activation. The top trace shows the command voltage indicating when the stimulus is presented. The second trace shows the extracellular neural recording. The three bottom traces (*x*, *y*, *z*) show the triaxial accelerometer recording of the stimulus. (a and b) Reprinted by permission from Springer Nature [22]. (c) Time series of action potentials in response to a 985 Hz bone-conducted vibration stimulus (shown by the gray acceleration trace). (d) Circular histogram of the phase of each spike. The Rayleigh test of circular uniformity was performed on the 142 spikes, and was significant ($P < 0.001$), showing that the time when an afferent is activated is phase-locked to a narrow band of phase angles of the 985 Hz stimulus. Here, the neuron misses many cycles, but the moment when the neuron fires is phase-locked (c and d). Reproduced with permission [8▪].

The effect of superior canal dehiscence on physiological responses

A hole in the bony wall of the guinea pig anterior canal (an SCD) of only 0.1 mm diameter causes anterior canal neurons with irregular resting activity to change from being unresponsive to ACS and BCV to having a very sensitive, phase-locked response, stimulus-locked to sound and vibration, as was shown by recordings from anterior canal neurons in guinea pigs before, during and after an SCD and then resealing the SCD [6▪], which eliminates the sound-evoked canal responses [7]. These neural changes are responsible for the reports of patients with SCD about sound-induced vertigo and are the foundation for the clinical tests of SCD, that is enhanced VEMP amplitudes to ACS or BCV. The enhanced VEMPs after SCD are explained by the SCD now allowing sound-activated SCC neurons to contribute to the generation of the VEMP, as well as otolith neurons [28▪,29] (Fig. 4). But there are also

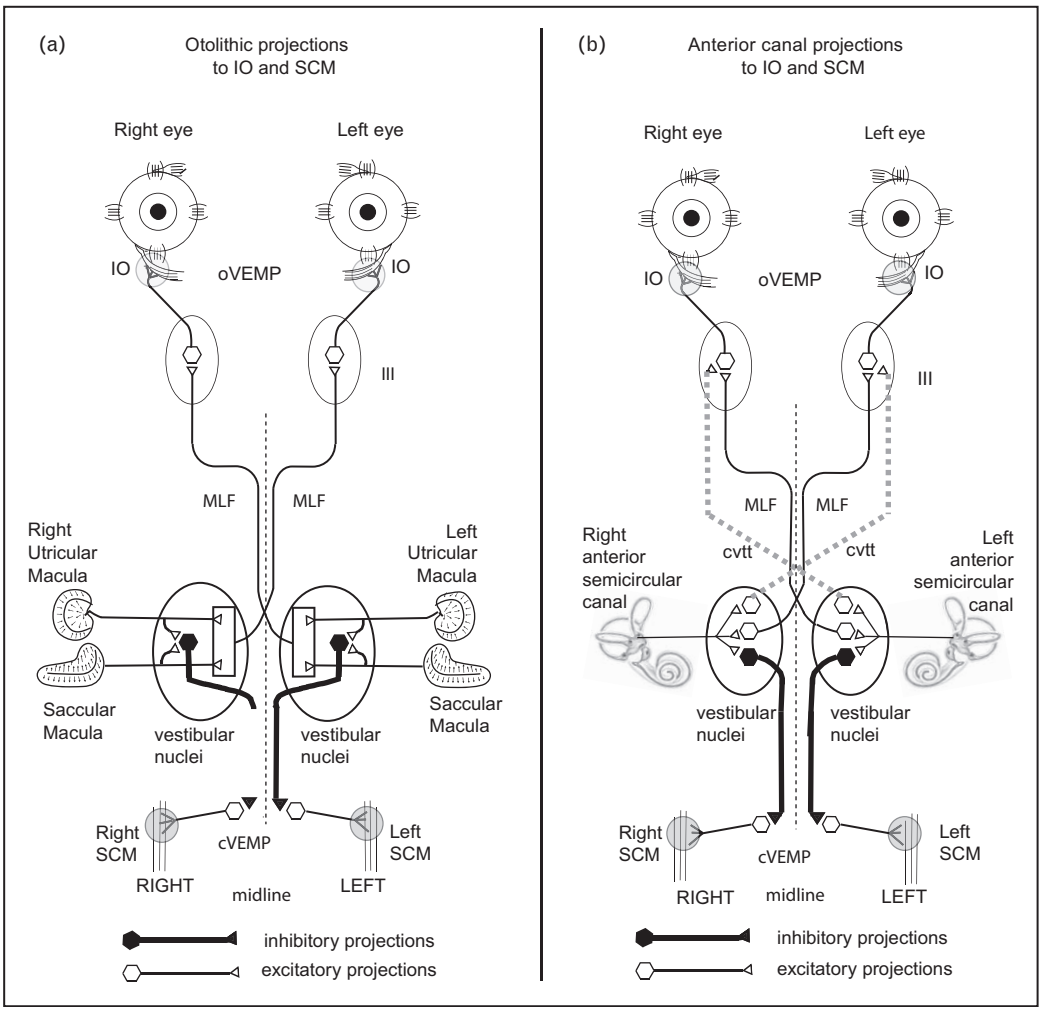

FIGURE 4. Schematic representations of otolithic (a) and anterior canal (b) projections to the inferior oblique eye muscle (IO) and the sternocleidomastoid (based on [29]). Part (a) shows some of the known otolithic vestibulo-ocular and vestibulo-collic neural projections that underlie the ocular and cervical vestibular-evoked myogenic potential. Afferents from the saccular and utricular macula project to the vestibular nuclei, but the exact termination of these afferents is not presently known, so this figure represents the present uncertainty about connections within the vestibular nuclei as an *open box*. MLF refers to the medial longitudinal fasciculus. The otolithic projections to other eye muscles are not shown. Afferents from the saccular macula synapse on an inhibitory neuron in the vestibular nucleus (*thick black lines*), projecting to spinal motoneurons controlling the sternocleidomastoid muscle. Part (b) shows anterior canal projections. cvtt refers to the crossed ventral tegmental tract. After superior canal dehiscence both otolithic and canal projections will operate causing enhanced ocular vestibular-evoked myogenic potentials and cervical vestibular-evoked myogenic potentials compared with healthy individuals. (a) Reprinted with permission [32]. (b) Reprinted by permission from Springer Nature [7].

enhanced responses to maintained ACS or BCV stimuli. These two aspects are accounted for by the cycle-by-cycle activation of previously unresponsive irregular canal afferents by the sound stimulus, and a generalized canal activation due to the maintained sound stimulus causing the cupula to be displaced. This occurs because ACS or BCV causes fluid flow in the dehiscent canal by an 'impedance pump' principle. In fluid dynamics, a rhythmic pulsing of a flexible tube in a closed-tube system can cause a unidirectional flow of the fluid filling the tube, depending on the impedance characteristics of the tube and on the frequency of the pulsing. This is the Liebau principle, and it is realized in pumps where there is no valve, but rhythmic pulsing causes a unidirectional flow of fluid [30▪,31▪▪]. In SCD, sound and vibration provide the rhythmic pulsing and cause a fluid flow and cupula displacement resulting in a steady activation of neurons, similar to that caused by an angular acceleration. Both mechanisms activate canal neurons and so would result in a maintained nystagmus to maintained sound after an SCD – the Tullio phenomenon [31▪▪].

Clinical methodology

VEMPs are not large and a number of techniques have been suggested to increase the signal-to-noise ratio – including different electrode configurations [33–35], a more powerful BCV stimulator [36], a new stimulus delivery system and analyser [37▪▪], a new stimulus (the chirp) [38], as well as different analytic techniques to enhance the signal-to-noise ratio [39,40]. However, changes to the standard protocol can sacrifice the otolithic specificity which is so valuable for VEMPs. For example, using low-frequency stimuli (rather than 500 Hz) has been reported as a way of improving VEMP amplitude [36,41,42], whereas the recent physiological evidence shows that low frequencies do not have the otolithic specificity of 500 Hz. Instead irregular SCC neurons can be activated by 100 Hz BCV [7]. The intensities used for generating VEMPs to ACS are high, and care is needed to minimize the noise dosage during testing [43,44]. Normative data about how VEMPs change with age are now available [45,46]. The probable path of stimulation of BCV through the skull and brain is still under investigation [42,47]. VEMPs to ACS in splenius capitis and masseter muscles have been reported, although the SCM is still the preferred recording site [48].

Clinical evidence and diagnostic relevance of vestibular-evoked myogenic potentials

VEMPs are nowadays widely used in the clinic for localization, differential diagnosis, monitoring and estimating the prognosis of vestibular disorders. They allow vestibular testing in patients with limited compliance, for example children (cVEMPs > 6 months, oVEMPs > 3 years) [49,50,51▪], and provide basic information about superior and inferior vestibular nerve function in patients not suitable for vestibulo–ocular reflex (VOR) testing (e.g. blindness, congenital nystagmus) [52▪,53].

One of the most important clinical applications of VEMPs is the confirmation of SCD, which tends to be overdiagnosed in high-resolution computed tomography of the temporal bone [54]. The most sensitive marker for SCD is a clearly increased contralateral oVEMP n10 amplitude (sensitivity: 100%; specificity: >90%) [55,56▪▪]. Diagnostic accuracy improves with rising stimulus frequencies for both oVEMP and cVEMP [40,57] which is in line with the phase-locked activation of anterior canal neurons in SCD up to several thousands of Hz [19]. Increase in VEMP amplitudes is less pronounced in patients with near-SCD as compared with those with a frank dehiscence [58▪].

VEMPs are indispensable for diagnosing isolated otolith dysfunction [27▪▪,59▪], an entity that particularly has to be considered in patients with balance disorders following concussion [60] or blast injury [61], adding further evidence to the noise susceptibility of otolithic receptors [62].

VEMP responses remain absent even years after permanent vestibular damage [63,64▪], but normalize during recovery of a vestibular disorder [65]. Therefore, VEMPs are helpful tools for monitoring dynamic otolithic function, for example, after vestibular neuritis, cochlear implantation [66,67] or intratympanic gentamicin treatment for Menière's disease [68].

In vestibular schwannomas, abnormal oVEMPs are associated with tumour origin in the superior vestibular nerve, whereas abnormal cVEMPs correlate with damage of the inferior vestibular nerve [69]. Preoperatively reduced cVEMP responses are linked to a higher risk for postoperative hearing loss (indicating involvement of the inferior vestibular nerve which is directly adjacent to the cochlear nerve), an important issue in patient counselling [70▪].

Reduced oVEMP (but not cVEMP) amplitudes predict recurrent disease in benign paroxysmal positional vertigo [71,72]. Successful repositioning of the otoliths results in recovery of oVEMP responses [73]. These findings indicate a specific role of utricular dysfunction in recurrent disease and help clinicians to identify those patients with risk of recurrence requiring a close follow-up.

VEMPs aid in the differential diagnosis of Menière's disease and vestibular migraine. In contrast to patients with vestibular migraine, Menière's disease patients frequently display a shift in frequency tuning from 500 to 1000 Hz for oVEMPs and cVEMPs [74–76]. The issue of age-matched controls is of paramount importance in studying VEMPs in Menière's disease, as an increase of VEMP best frequency is also observed for normal controls above the age of 60 [77,78]. Vestibular migraine patients typically show abnormal oVEMPs with preserved cVEMPs [79].

It cannot be emphasized enough that VEMPs reflect not only peripheral otolithic function, but also the integrity of central vestibulo–spinal and vestibulo–ocular pathways and the effector muscles (SCM or inferior oblique eye muscle). One important new clinical application of this principle is the decrement of the oVEMP n10 amplitude during repetitive stimulation in patients with ocular myasthenia gravis, which might also be a useful tool for monitoring treatment efficacy [80,81▪▪]. Moreover, VEMPs are abnormal in a number of neurological disorders with brainstem involvement [82], such as multiple sclerosis (MS) [83,84], Parkinson's disease [85], amyotrophic lateral sclerosis [86] or idiopathic rapid eye movement sleep behavioural disorders [87▪], adding information to the pathophysiology

of these disorders, in particular the role of central vestibular circuits. Prolonged oVEMP n10 and cVEMP p13 latencies predict a higher risk for falls in MS patients [88▪].

Finally, recent research indicates a correlation between otolithic – in particular saccular – and cognitive function [89▪▪]. Alzheimer's disease is three times more likely in elderly individuals with bilateral absent cVEMP responses. Among those patients with Alzheimer's disease, reduced cVEMP amplitudes are associated with poorer spatial cognition.

VIBRATION-INDUCED NYSTAGMUS

Anatomical and physiological basis

The new physiological evidence has provided the scientific basis for a simple screening test of the asymmetry of labyrinthine function – vibration-induced nystagmus (VIN) [90,91]. A 100-Hz vibration applied to either mastoid in patients with unilateral vestibular loss immediately elicits a mainly horizontal nystagmus which lasts as long as the stimulus is applied. Recent physiology shows that while 500 Hz is selective for otoliths, 100 Hz BCV does activate irregular SCC afferents in healthy animals with normally encased labyrinths [7], and they fire in a cycle-by-cycle basis so that 100 Hz vibration causes a firing rate of 100 spikes/s, probably similar to that caused by a modest angular acceleration. This cycle-by-cycle activation of single canal afferent neurons to 100 Hz stimulation explains the abrupt start and stop of VIN and the lack of adaptation during the stimulus, and the lack of aftereffects after the end of the stimulus [90].

Clinical application

Because of the very efficient transmission of vibration through the skull and brain, 100 Hz vibration of one mastoid activates canal afferents in both labyrinths, and in healthy individuals those two neural signals probably cancel each other at the vestibular nucleus, so there is no nystagmus. However, in patients with asymmetrical canal function, 100 Hz BCV of either mastoid causes irregular afferents from the intact labyrinth to be activated, but there is no central cancellation from the other (absent) labyrinth. As a result, vibration generates a nystagmus with a very rapid onset and abrupt offset and with quick phases beating away from the lesioned side [90,92]. Like VEMPs, unilateral loss causes a permanent VIN. If there is an SCD then the afferents on the side of the SCD have a stronger response (see above) than afferents on the intact side, with the result that the nystagmus beats *towards* the side with the SCD [90,92]. In patients with an SCD, the nystagmus can be elicited up to high frequencies (750 Hz or more).

THE EVOLUTIONARY CONUNDRUM

Why do otolith receptors respond to sound and vibration? Otolithic receptors and afferents in fish detect the presence and direction of vibration to warn of the direction of predators [93,94]. The mammalian calyx afferent terminal may have evolved in mammals to improve the temporal precision of vestibular afferents as head movements became less constrained in air rather than water [16,19].

CONCLUSION

VEMPs should be part of the standard neurotological test battery as they are the only test able to diagnose isolated dynamic otolithic dysfunction. They complement – rather than replace – other vestibular tests in many other peripheral vestibular disorders, for example SCD and Menière's disease, and are a diagnostic alternative if VOR testing is not possible (see above). Promising new clinical applications include myasthenia gravis, neurological disease with brainstem involvement and cognitive disorders. VIN is particularly useful to detect asymmetric canal function in patients where head impulse testing cannot be performed (e.g. restricted neck movement) [90].

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None.

Conflicts of interest

I.S.C. is an unpaid consultant to GN Otometrics (Taastrup, Denmark), but has received support from GN Otometrics for travel and attendance at conferences and workshops. J.D. has received speaker's honoraria from GN Otometrics. I.S.C. is in receipt of a conjoint grant from the Garnett Passe and Rodney Williams Memorial Foundation.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:
- ▪ of special interest
- ▪▪ of outstanding interest

1. Straka H, Zwergal A, Cullen KE. Vestibular animal models: contributions to understanding physiology and disease. J Neurol 2016; 263:S10–S23.

2. Fritzsch B, Straka H. Evolution of vertebrate mechanosensory hair cells and inner ears: toward identifying stimuli that select mutation driven altered morphologies. J Comp Physiol A Neuroethol Sens Neural Behav Physiol 2014; 200:5–18.
3. Géléoc GSG, Lennan GWT, Richardson GP, Kros CJ. A quantitative comparison of mechanoelectrical transduction in vestibular and auditory hair cells of neonatal mice. Proc Biol Sci 1997; 264:611–621.
4. Curthoys IS, Vulovic V, Burgess AM, *et al.* The response of guinea pig primary utricular and saccular irregular neurons to bone-conducted vibration (BCV) and air-conducted sound (ACS). Hear Res 2016; 331:131–143.
5. ■ Curthoys IS, Grant JW, Pastras CJ, *et al.* A review of mechanical and synaptic processes in otolith transduction of sound and vibration for clinical VEMP testing. J Neurophysiol 2019; 122:259–276.

This is a summary of much anatomical and physiological evidence explaining how otolithic receptors can be activated and phase lock to the individual cycles of such high frequencies of sound and vibration (>2000 Hz).

6. ■ Dlugaiczyk J, Burgess AM, Goonetilleke SC, *et al.* Superior canal dehiscence syndrome: relating clinical findings with vestibular neural responses from a guinea pig model. Otol Neurotol 2019; 40:E406–E414.

The article presents the neurophysiological foundation for increased vestibular-evoked myogenic potential (VEMP) responses in superior canal dehiscence (SCD): anterior canal neurons with irregular resting discharge firing in addition to otolithic neurons during application of air-conducted sound (ACS) or bone-conducted vibration (BCV).

7. Curthoys IS. The new vestibular stimuli: sound and vibration – anatomical, physiological and clinical evidence. Exp Brain Res 2017; 235:957–972.
8. ■ Curthoys IS, Grant JW, Burgess AM, *et al.* Otolithic receptor mechanisms for vestibular-evoked myogenic potentials: a review. Front Neurol 2018; 9:366.

The article summarizes some of the evidence for the two streams of neural output from the otoliths.

9. Dlugaiczyk J. Ocular vestibular evoked myogenic potentials: where are we now? Otol Neurotol 2017; 38:E513–E521.
10. ■■ Rosengren SM, Colebatch JG. The contributions of vestibular evoked myogenic potentials and acoustic vestibular stimulation to our understanding of the vestibular system. Front Neurol 2018; 9:481.

An excellent review about the history of VEMPs and the lessons learned from animal and human studies with this technique.

11. ■■ Rosengren SM, Colebatch JG, Young AS, *et al.* Vestibular evoked myogenic potentials in practice: methods, pitfalls and clinical applications. Clin Neurophysiol Pract 2019; 4:47–68.

The authors share their abundant knowledge about pearls and pitfalls in recording, analyzing and interpreting VEMPs with the reader, and show illustrative clinical examples of VEMPs in synopsis with other vestibular tests. A must-read for everyone dealing with VEMPs in clinical practice!

12. Fife TD, Colebatch JG, Kerber KA, *et al.* Practice guideline: cervical and ocular vestibular evoked myogenic potential testing. Report of the guideline development, dissemination, and implementation subcommittee of the American Academy of Neurology. Neurology 2017; 89:2288–2296.
13. ■■ Papathanasiou E, Straumann D. Why and when to refer patients for vestibular evoked myogenic potentials: a critical review. Clin Neurophysiol 2019; 130:1539–1556.

The authors give a very detailed and comprehensive account of the clinical use of VEMPs in a variety of peripheral and central vestibular disorders, in particular highlighting their additional diagnostic value compared with other tests. Furthermore, the authors make valuable suggestions for further clinical research and suggest minimal standards for reporting VEMPs in scientific publications.

14. Papathanasiou ES, Murofushi T, Akin FW, Colebatch JG. International guidelines for the clinical application of cervical vestibular evoked myogenic potentials: an expert consensus report. Clin Neurophysiol 2014; 125:658–666.
15. Iwasaki S, Chihara Y, Smulders YE, *et al.* The role of the superior vestibular nerve in generating ocular vestibular-evoked myogenic potentials to bone conducted vibration at Fz. Clin Neurophysiol 2009; 120:588–593.
16. Eatock RA. Specializations for fast signaling in the amniote vestibular inner ear. Integr Comp Biol 2018; 58:341–350.
17. ■■ Nam JH, Grant JW, Rowe MH, Peterson EH. Multiscale modeling of mechanotransduction in the utricle. J Neurophysiol 2019; 122:132–150.

An excellent, up-to-date review about the biomechanical foundations of utricular function in general and the two streams of otolithic information in particular.

18. Curthoys IS, MacDougall HG, Vidal PP, de Waele C. Sustained and transient vestibular systems: a physiological basis for interpreting vestibular function. Front Neurol 2017; 8:117.
19. Curthoys IS, Burgess AM, Goonetilleke SC. Phase-locking of irregular guinea pig primary vestibular afferents to high frequency (>250 Hz) sound and vibration. Hear Res 2019; 373:59–70.
20. Pastras CJ, Curthoys IS, Brown DJ. In vivo recording of the vestibular microphonic in mammals. Hear Res 2017; 354:38–47.
21. Pastras CJ, Curthoys IS, Brown DJ. Dynamic response to sound and vibration of the guinea pig utricular macula, measured in vivo using Laser Doppler Vibrometry. Hear Res 2018; 370:232–237.
22. Curthoys IS, Vulovic V. Vestibular primary afferent responses to sound and vibration in the guinea pig. Exp Brain Res 2011; 210:347–352.
23. Grant W, Curthoys I. Otoliths – accelerometer and seismometer; implications in vestibular evoked myogenic potential (VEMP). Hear Res 2017; 353: 26–35.
24. ■■ Dieterich M, Brandt T. Perception of verticality and vestibular disorders of balance and falls. Front Neurol 2019; 10:172.

An excellent comprehensive review about perception of verticality in general and clinical application of the subjective visual vertical in particular.

25. Lyford-Pike S, Vogelheim C, Chu E, *et al.* Gentamicin is primarily localized in vestibular type I hair cells after intratympanic administration. J Assoc Res Otolaryngol 2007; 8:497–508.
26. ■■ Cherchi M. Utricular function in vestibular neuritis: a pilot study of concordance/discordance between ocular vestibular evoked myogenic potentials and ocular cycloposition. Exp Brain Res 2019; 237:1531–1538.

The authors use a very clever approach to show that tests of sustained and transient otolithic function [ocular torsion vs. ocular VEMPs (oVEMPs)] do not need to display the same results in patients with vestibular neuritis. Thus, this article provides very powerful clinical evidence for the two different streams of otolithic function.

27. ■■ Park HG, Lee JH, Oh SH, *et al.* Proposal on the diagnostic criteria of definite isolated otolith dysfunction. J Audiol Otol 2019; 23:103–111.

The authors propose useful criteria for symptoms-based and lab-based diagnosis of isolated otolith dysfunction, although excluding rotatory vertigo from the characteristic clinical symptoms is debatable (see also Fujimoto et al. [59■]).

28. ■ Corneil BD, Camp AJ. Animal models of vestibular evoked myogenic potentials: the past, present, and future. Front Neurol 2018; 9:489.

An overview of the basic physiology of VEMPs.

29. Uchino Y, Kushiro K. Differences between otolith- and semicircular canal-activated neural circuitry in the vestibular system. Neurosci Res 2011; 71:315–327.
30. ■ Iversen MM, Zhu H, Zhou W, *et al.* Sound abnormally stimulates the vestibular system in canal dehiscence syndrome by generating pathological fluid-mechanical waves. Sci Rep 2018; 8:10257.

The basic evidence explaining why SCD occurs.

31. ■■ Rabbitt RD. Semicircular canal biomechanics in health and disease. J Neurophysiol 2019; 121:732–755.

An outstanding coverage of the mechanical operation and the neurophysiology of the semicircular canals (SCCs), including results and modelling of SCD.

32. Curthoys IS, Vulovic V, Burgess AM, *et al.* The basis for using bone-conducted vibration or air-conducted sound to test otolithic function. Ann N Y Acad Sci 2011; 1233:231–241.
33. Leyssens L, Heinze B, Vinck B, *et al.* 'Standard' versus 'nose reference' electrode placement for measuring oVEMPs with air-conducted sound: test–retest reliability and preliminary patient results. Clin Neurophysiol 2017; 128:312–322.
34. Vanspauwen R, Wuyts FL, Krijger S, Maes LK. Comparison of different electrode configurations for the oVEMP with bone-conducted vibration. Ear Hear 2017; 38:205–211.
35. Piker EG, Jacobson GP, Makowiec KF, *et al.* The medial canthus reference electrode is not electrically indifferent to the ocular vestibular evoked myogenic potential. Otol Neurotol 2018; 39:E1069–E1077.
36. Håkansson B, Jansson KJF, Tengstrand T, *et al.* VEMP using a new low-frequency bone conduction transducer. Med Devices (Auckl) 2018; 11:301–312.
37. ■■ MacDougall HG, Holden J, Rosengren SM, Chiarovano E. μVEMP: a portable interface to record vestibular evoked myogenic potentials (VEMPs) with a smart phone or tablet. Front Neurol 2018; 9:543.

Description of a very small and portable device for recording cervical VEMP (cVEMP) and oVEMP with ACS and BCV, which makes it possible to test dynamic otolithic function almost everywhere.

38. Cebulla M, Walther LE. Cervical vestibular evoked myogenic potentials via air conduction delivered by either sequentially or quasi-simultaneously presented narrow-band chirp stimuli. Int J Audiol 2019; 58:174–179.
39. Noij KS, van Tilburg MJ, Herrmann BS, *et al.* Toward optimizing VEMP: calculating VEMP inhibition depth with a generic template. Ear Hear 2018; 39:1199–1206.
40. Noij KS, Herrmann BS, Guinan JJ, Rauch SD. Toward optimizing cVEMP: 2,000-Hz tone bursts improve the detection of superior canal dehiscence. Audiol Neurootol 2018; 23:335–344.
41. Holmeslet B, Klaksvik J, Goplen F, *et al.* The repeatability of oVEMP in response to low-frequency vibration against the vertex and forehead. J Vestib Res 2016; 26:303–309.
42. Verrecchia L, Westin M, Duan ML, Brantberg K. Ocular vestibular evoked myogenic potentials to vertex low frequency vibration as a diagnostic test for superior canal dehiscence. Clin Neurophysiol 2016; 127:2134–2139.
43. Portnuff CDF, Kleindienst S, Bogle JM. Safe use of acoustic vestibular-evoked myogenic potential stimuli: protocol and patient-specific considerations. J Am Acad Audiol 2017; 28:708–717.
44. Colebatch JG, Rosengren SM. Safe levels of acoustic stimulation for VEMPs: comment on 'Sudden bilateral hearing loss after cervical and ocular vestibular evoked myogenic potentials'. Otol Neurotol 2016; 37:117–118.
45. Singh NK, Firdose H. Characterizing the age and stimulus frequency interaction for ocular vestibular-evoked myogenic potentials. Ear Hear 2018; 39:251–259.

46. Brix GS, Ovesen T, Devantier L. Vestibular evoked myogenic potential in healthy adolescents. Int J Pediatr Otorhinolaryngol 2019; 116:49–57.
47. Govender S, Colebatch JG. Location and phase effects for ocular and cervical vestibular-evoked myogenic potentials evoked by bone-conducted stimuli at midline skull sites. J Neurophysiol 2018; 119:1045–1056.
48. Rosengren SM, Weber KP, Govender S, *et al.* Sound-evoked vestibular projections to the splenius capitis in humans: comparison with the sternocleidomastoid muscle. J Appl Physiol 2019; 126:1619–1629.
49. Janky KL, Rodriguez AI. Quantitative vestibular function testing in the pediatric population. Semin Hear 2018; 39:257–274.
50. Rodriguez AI, Thomas MLA, Janky KL. Air-conducted vestibular evoked myogenic potential testing in children, adolescents, and young adults: thresholds, frequency tuning, and effects of sound exposure. Ear Hear 2019; 40:192–203.
51. ▪ Martens S, Dhooge I, Dhondt C, *et al.* Vestibular infant screening – Flanders: the implementation of a standard vestibular screening protocol for hearing-impaired children in Flanders. Int J Pediatr Otorhinolaryngol 2019; 120: 196–201.

A very useful account about screening vestibular function even in very young hearing-impaired children with cVEMPs.

52. ▪ Bayram A, Kalkan M, Unsal N, *et al.* Does blindness affect ocular vestibular evoked myogenic potentials? Am J Otolaryngol 2018; 39:290–292.

Evidence that blindness does not affect oVEMP responses as long as the extraocular eye muscles are intact. These results are the basis for using oVEMPs as a test for superior vestibular nerve function in blind persons where videooculographic recordings are often not possible/useful.

53. Manzari L, Burgess AM, Curthoys IS. Is it possible to measure peripheral vestibular function in a patient with congenital nystagmus? Eur Arch Otorhinolaryngol 2012; 269:349–352.
54. Ward BK, Carey JP, Minor LB. Superior canal dehiscence syndrome: lessons from the first 20 years. Front Neurol 2017; 8:177.
55. Janky KL, Nguyen KD, Welgampola M, *et al.* Air-conducted oVEMPs provide the best separation between intact and superior canal dehiscent labyrinths. Otol Neurotol 2013; 34:127–134.
56. ▪▪ Verrecchia L, Brantberg K, Tawfique Z, Maoli D. Diagnostic accuracy of ocular vestibular evoked myogenic potentials for superior canal dehiscence syndrome in a large cohort of dizzy patients. Ear Hear 2019; 40:287–294.

This is the first study from a large sample of dizzy patients showing that elevated oVEMP responses are able to separate SCD from other causes of vertigo/dizziness.

57. Manzari L, Burgess AM, McGarvie LA, Curthoys IS. An indicator of probable semicircular canal dehiscence: ocular vestibular evoked myogenic potentials to high frequencies. Otolaryngol Head Neck Surg 2013; 149:142–145.
58. ▪ Baxter M, McCorkle C, Guajardo CT, *et al.* Clinical and physiologic predictors and postoperative outcomes of near dehiscence syndrome. Otol Neurotol 2019; 40:204–212.

Very good characterization of audiovestibular findings in patients with a thinning of the bony roof of the superior canal as opposed to those with a frank bony dehiscence. The results of this article support the notion that SCD/near-SCD is a spectrum of disorders with very different clinical presentations.

59. ▪ Fujimoto C, Suzuki S, Kinoshita M, *et al.* Clinical features of otolith organ-specific vestibular dysfunction. Clin Neurophysiol 2018; 129:238–245.

The authors show that abnormal cVEMP and oVEMP can occur although tests of SCC function are normal, thus highlighting the importance of isolated otolithic disorders, a so far neglected clinical entity.

60. Akin FW, Murnane OD, Hall CD, Riska KM. Vestibular consequences of mild traumatic brain injury and blast exposure: a review. Brain Inj 2017; 31:1188–1194.
61. Liao YH, Young YH. Inner ear damage by firecracker trauma. Audiol Neurootol 2018; 23:116–121.
62. Stewart CE, Kanicki AC, Altschuler RA, King WM. Vestibular short-latency evoked potential abolished by low-frequency noise exposure in rats. J Neurophysiol 2018; 119:662–667.
63. Iwasaki S, Smulders YE, Burgess AM, *et al.* Ocular vestibular evoked myogenic potentials in response to bone-conducted vibration of the midline forehead at Fz. A new indicator of unilateral otolithic loss. Audiol Neurootol 2008; 13:396–404.
64. ▪ Canale A, Caranzano F, Lanotte M, *et al.* Comparison of VEMPs, VHIT and caloric test outcomes after vestibular neurectomy in Meniere's disease. Auris Nasus Larynx 2018; 45:1159–1165.

The study in 15 patients following unilateral unilateral vestibular neurectomy shows that oVEMP and cVEMP of the affected side are absent even 12 years after surgery adding further evidence to the observation that tests of transient vestibular function are not affected by vestibular compensation.

65. Hu J, Wang H, Chen Z, *et al.* Recovery of ocular and cervical vestibular evoked myogenic potentials after treatment of inner ear diseases. Int J Neurosci 2019; 129:1004–1012.
66. Miwa T, Minoda R, Matsuyoshi H, Takeda H. The effect of cochlear implants on vestibular-evoked myogenic potential responses and postural stability. Auris Nasus Larynx 2019; 46:50–57.
67. Colin V, Bertholon P, Roy S, Karkas A. Impact of cochlear implantation on peripheral vestibular function in adults. Eur Ann Otorhinolaryngol Head Neck Dis 2018; 135:417–420.
68. Yetişer S. Intratympanic gentamicin for intractable Meniere's Disease – a review and analysis of audiovestibular impact. Int Arch Otorhinolaryngol 2018; 22:190–194.
69. Rahne T, Plossl S, Plontke SK, Strauss C. Preoperative determination of nerve of origin in patients with vestibular schwannoma. HNO 2018; 66:16–21.
70. ▪ Hochet B, Achard S, Lorenz MB, *et al.* Preoperative assessment of cervical vestibular evoked myogenic potentials (cVEMPs) help in predicting hearing preservation after removal of vestibular schwannomas through a middle fossa craniotomy. Otol Neurotol 2018; 39:e1143–e1149.

The article highlights the predictive value of cVEMPs for hearing preservation after vestibular schwannoma surgery – a very important issue in patient counselling.

71. Martínez Pascual P, Amaro Merino P. Otolithic damage study in patients with benign paroxysmal positional vertigo with vestibular evoked myogenic potentials. Acta Otorrinolaringol Esp 2019; 70:131–135.
72. Chen G, Zhao X, Yu G, *et al.* Otolith dysfunction in recurrent benign paroxysmal positional vertigo after mild traumatic brain injury. Acta Otolaryngol 2019; 139:18–21.
73. Asal S, Sobhy O, Balbaa A. oVEMP as an objective indicator of successful repositioning maneuver. Acta Otorrinolaringol Esp 2018; 69:141–148.
74. Murofushi T, Tsubota M, Suizu R, Yoshimura E. Is alteration of tuning property in cervical vestibular-evoked myogenic potential specific for Meniere's disease? Front Neurol 2017; 8:193.
75. Maxwell R, Jerin C, Gurkov R. Utilisation of multifrequency VEMPs improves diagnostic accuracy for Meniere's disease. Eur Arch Otorhinolaryngol 2017; 274:85–93.
76. Maheu M, Alvarado-Umanzor JM, Delcenserie A, Champoux F. The clinical utility of vestibular-evoked myogenic potentials in the diagnosis of Meniere's disease. Front Neurol 2017; 8:415.
77. Obeidat FS, Bell SL. Comparing the sensitivity and specificity of cervical vestibular-evoked myogenic potentials and electrocochleography in the diagnosis of Meniere's disease. Int J Audiol 2019; 58:738–746.
78. Piker EG, Jacobson GP, Burkard RF, *et al.* Effects of age on the tuning of the cVEMP and oVEMP. Ear Hear 2013; 34:e65–e73.
79. Makowiec KF, Piker EG, Jacobson GP, *et al.* Ocular and cervical vestibular evoked myogenic potentials in patients with vestibular migraine. Otol Neurotol 2018; 39:e561–e567.
80. Valko Y, Rosengren SM, Jung HH, *et al.* Ocular vestibular evoked myogenic potentials as a test for myasthenia gravis. Neurology 2016; 86:660–668.
81. ▪▪ Wirth MA, Valko Y, Rosengren SM, *et al.* Repetitive ocular vestibular evoked myogenic potential stimulation for the diagnosis of myasthenia gravis: optimization of stimulation parameters. Clin Neurophysiol 2019; 130: 1125–1134.

The study presents a very intelligent new application of oVEMPs: a decrement of the oVEMP n10 amplitude during repeated stimulation indicates ocular myasthenia gravis.

82. Oh SY, Kim HJ, Kim JS. Vestibular-evoked myogenic potentials in central vestibular disorders. J Neurol 2016; 263:210–220.
83. Kavasoğlu G, Gökçay F, Yüceyar N, Çelebisoy N. Cervical vestibular-evoked myogenic potentials in patients with multiple sclerosis: sensitive in detecting brainstem involvement? Neurol Sci 2018; 39:365–371.
84. Di Stadio A, Dipietro L, Ralli M, *et al.* The role of vestibular evoked myogenic potentials in multiple sclerosis-related vertigo. A systematic review of the literature. Mult Scler Relat Disord 2019; 28:159–164.
85. Smith PF. Vestibular functions and Parkinson's disease. Front Neurol 2018; 9:1085.
86. Liu X, Zhang S, Huang X, *et al.* Vestibular evoked myogenic potentials and their clinical utility in patients with amyotrophic lateral sclerosis. Clin Neurophysiol 2019; 130:647–654.
87. ▪ de Natale ER, Ginatempo F, Laccu I, *et al.* Vestibular evoked myogenic potentials are abnormal in idiopathic REM sleep behavior disorder. Front Neurol 2018; 9:911.

A very interesting example of using VEMPs for analysing brainstem function in neurological disease.

88. ▪ Chinnadurai SA, Gandhirajan D, Srinivasan AV, *et al.* Predicting falls in multiple sclerosis: do electrophysiological measures have a better predictive accuracy compared to clinical measures? Mult Scler Relat Disord 2018; 20:199–203.

This is a new and very useful application of VEMPs in patients with multiple sclerosis (MS). Prolonged cVEMP and oVEMP latencies predict falls better than clinical measures. The results of this study have important implications for falls prevention in MS patients.

89. ▪▪ Agrawal Y, Smith PF, Rosenberg PB. Vestibular impairment, cognitive decline and Alzheimer's disease: balancing the evidence. Aging Ment Health 2019; 1–4; in press. doi: 10.1080/13607863.2019.1566813.

An up-to-date and comprehensive review of data from animal experiments and clinical studies supporting a connection between vestibular – in particular saccular – impairment and cognitive decline. This is a new field in vestibular research with big implications in an aging society.

90. Dumas G, Curthoys IS, Lion A, *et al.* The skull vibration-induced nystagmus test of vestibular function – a review. Front Neurol 2017; 8:41.

91. Zamora EG, Araujo PES, Guillen VP, *et al.* Parameters of skull vibration-induced nystagmus in normal subjects. Eur Arch Otorhinolaryngol 2018; 275:1955–1961.
92. Dumas G, Tan HS, Perrin P, *et al.* Skull vibration induced nystagmus in patients with superior semicircular canal dehiscence. Eur Ann Otorhinolaryngol Head Neck Dis 2019; 136:263–272.
93. Edds-Walton PL. What the toadfish ear tells the toadfish brain about sound. Adv Exp Med Biol 2016; 877:197–226.
94. Zeddies DG, Fay RR, Gray MD, *et al.* Local acoustic particle motion guides sound-source localization behavior in the plainfin midshipman fish, *Porichthys notatus*. J Exp Biol 2012; 215:152–160.